REMARKS

Large Entity Status

Applicants note that according to the PAIR website, a letter was filed by Mr. Alexander Powell on August 28, 2006, erroneously requesting a change in record to reflect a small entity status for application No. 10/525,348. A copy of this letter is attached as Exhibit 1. Upon a closer examination of Mr. Powell's letter, including the attachment, it is clear that Mr. Powell refers to Application No. 10/525,548, entitled "An Elevator System," not Application No. 10/525,348. Applicant respectfully requests that the Office remove Mr. Powell's letter from the files of the present application (10/525,348). Applicant also hereby affirms that the records of the present application should reflect Large Entity status, not Small Entity status.

Claim Amendments

Claims 1, 19, and 26 have been amended. Claims 1, 19 and 26 now recite "...pantethine, cysteamine, and epigallocatechin gallate (EGCG)" rather than "...pantethine or a metabolite thereof, EGCG, phytanic acid, lipoic acid and poliocosanol." Support for the amendment may be found, for example, in original claim 1 and in the specification, at for example, page 4, line 27 and page 5, line 13. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claim 26 has also been amended to recite "treatment of type 2 diabetes, and for the prevention of type 2 diabetes" rather than "treatment of both type 1 and 2

diabetes, and for the prevention of type 2 diabetes." Support for this amendment may be found, for example, in original claim 26. (Id.)

Claims 2, 7-12, 20-25 and 27 have been cancelled, without prejudice.

Indefiniteness Rejection

Claims 1-2, 5-6, 20 and 26-27 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter. (Paper No. 20070723 at 2). In making the rejection, the Examiner asserted that "[t]he abbreviation 'EGCG' is not spelled out in the claims or disclosure and is therefore vague and indefinite." (*Id.*)

With respect to the assertion that the abbreviation "EGCG" is not spelled out in the disclosure, the applicants respectfully direct the Examiner's attention to page 4, line 27 of the specification, which reads, "EGCG: Epigallocatechin gallate (ECGC) ..." With respect to the use of the abbreviation "EGCG" in the claims, independent claims 1 and 26 have been amended to recite "epigallocatechin gallate (EGCG)." In addition, claims 2, 20 and 27 have been cancelled, which renders the rejection moot as to those claims. Thus, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

Written Description Rejection

Claims 1-2 and 26-27 were rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to convey that the inventors, at the time the application was filed, had possession of the claimed invention. (Paper No. 20070723 at 2-3). In making the rejection, the Examiner acknowledged that the application "does provide adequate written description for panthethine and one metabolite of panthethine—cysteamin[e]." (*Id.*) The Examiner, however, asserted that "other metabolites of panthethine are not adequately described." (*Id.* at 3).

With a view towards furthering prosecution, claims 1 and 26 have been amended to recite "cysteamine" rather than a metabolite of pantethine. Furthermore, claim 27 has been cancelled, rendering the rejection moot as to this claim. For the foregoing reasons, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

Enablement Rejection

Claims 26 and 27 were rejected under 35 USC § 112, first paragraph, on the asserted grounds that the specification is not enabling for "1) the treatment of type 1 diabetes, or for 2) the prevent[ion of] type 2 diabetes in those individuals with pre-diabetes, impaired glucose tolerance or obesity." (*Id.* at 3).

With a view towards furthering prosecution, claim 27 has been cancelled. Therefore, the rejection has been rendered moot with respect to claim 27. With respect to claim 26, the rejection is respectfully traversed in part as set forth below.

a. Treatment of Type I Diabetes

In making the rejection of claim 26, the Examiner asserted that [n]o working examples for treatment of type 1 diabetes are presented" and that "[g]iven the different underlying causes of type 1 and type 2 diabetes, one of skill in the art would have no guidance as to how to treat type 1 diabetes." (*Id.* at 5) The Examiner further asserted that "[g]iven the complete absence of insulin production in type 1 diabetics, compounds that act to increase the activity of cells to insulin would not be expected to have an effect." (*Id.* at 5-6). Thus, the Examiner concluded that "the claims as they relate to the treatment of type 1 diabetes lack enablement." (*Id.* at 6).

With a view towards further prosecution, claim 26 has been amended to cancel the recitation of "type 1 diabetes." Therefore, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

b. Prevention of Type II Diabetes

The Examiner acknowledged that the specification is "enabling for **treating** type 2 diabetes in those individuals with pre-diabetes, impaired glucose tolerance or obesity." (Paper No. 20070723 at 3) (emphasis added). The Examiner, however, asserted that "the claims as they relate to the **prevention** of type 2 diabetes lack enablement.." (*Id.* at 7). In making the rejection, the Examiner asserted that "[t]he verb "prevent" is defined to mean "to stop (someone or something) from ... being in a

certain state" ('prevent' from dictionary.com, accessed Aug 2, 2007), i.e. to complete [sic] eliminate a certain state." (Id. at 6). The Examiner also asserted that "no working examples for the use of the claimed composition in the prevention of type 2 diabetes are shown." (*Id.* at 6-7). The Examiner further asserted that "no drug has been shown that can bring the progression of the disease to a halt and prevent them from developing diabetes" and that the "application does not provide any evidence as to the efficacy of the composition in...model systems that prevents the appearance of type 2 diabetes." (*Id.* at 7).

It is respectfully submitted that the Examiner's acknowledgment that the specification enables treatment of Type 2 diabetes is also a concession that prevention of Type 2 diabetes is also enabled. As is well known in the art, "Type 2 diabetes can be prevented or dealyed." Diabetes Care, 25(4): 742-749, 747 (2002). Indeed the co-authors of this article sponsored by the American Diabetes Association and the NIDDKD acknowledge that "conceptually, 'prevention' is no different from 'treatment'...." *Id.* at 746. Moreover, the American Diabetes Association on its website (a copy of which is attached as Exhibit 2) proclaims that "research has also shown that if you take action to control your blood glucose when you have pre-diabetes, you can delay or prevent type 2 diabetes from ever developing."

In Examples 12 and 13, blood glucose control is demonstrated by the use of the presently claimed compositions. (pages 19-22). In Example 12, various compositions were tested in a db/db mouse model of diabetes. The blood glucose levels in mice treated with certain combinations of compounds were lower than the

control groups. In other words, treated mice have better glucose tolerance and blood glucose control compared to the untreated mice. Individuals with pre-diabetes would clearly benefit from the synergistic effects of increased glucose control demonstrated in the db/db mouse model. Example 13 similarly demonstrates the ability of the instantly claimed composition in glucose control. The compositions tested down-regulated the expression of one of the major glucose-metabolism rate-limiting enzymes. One skilled in this art would conclude from this example that the test compositions are useful in the reduction of glucose output and "prevent diabetes." (Page 22, line 22).

Thus, because the specification discloses how to control glucose levels, both prevention and treatment of type 2 diabetes are enabled. The specification also provides examples and evidence that the compositions recited in the claims prevent the appearance of type 2 diabetes in model systems.

In view of the foregoing it is respectfully submitted that the rejection as to claim 26 and preventing diabetes Type 2 has been rendered moot and should be withdrawn.

Anticipation Rejections

a. Reddi

Claims 13, 16 and 17 were rejected under 35 USC 102(b) as anticipated by Reddi *et al.* (Life Sciences, Vol 42, p 1323-1330, 1998) ("Reddi"). (Paper No. 20070723 at 7). In making the rejection, the Examiner asserted only that Reddi

discloses administration of biotin that "falls within the range" of the biotin dosage recited in claims 1 and 17. (*Id.* at 7-8).

As is well settled, anticipation requires "identity of invention." *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply,* 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.,* 221 USPQ 481, 485 (Fed. Cir 1984).

Claims 13, 16 and 17 depend from claim 1, which recites a **combination** of biotin and panthethine, biotin and cysteamine, or biotin and EGCG. The rejection fails to identify any disclosure in Reddi of any such combination. Indeed, the later rejections under §103(a) concede that Reddi does ***not*** disclose any of the combinations recited by the claims. (*See, e.g.*, Paper No. 20070723 at 10-12.) Thus, each and every element of claims 13, 16 and 17 is not disclosed by Reddi. Accordingly, the rejection is deficient as a matter of fact and law and should be withdrawn.

b. Coggeshalle

Claims 13-15 were rejected under 35 USC § 102(b) as being anticipated by Coggeshalle *et al.* (Ann N.Y. Acad Sci, 447, p 389-392, 1985) ("Coggeshalle"). (Paper No. 20070723 at 8). In making the rejection, the Examiner asserted that Coggeshall "uses a solid tablet (p 392, ln 12) containing 16 mg/day of biotin (p 389, lns 16-17) which anticipates the claims of the instant application of a solid dosage form and one that contains about 0.35 mg to 200 mg of biotin."

Claims 13-15 depend from claim 1 and thus incorporate all the limitations of claim 1 which recites a combination of (a) biotin and (b) either panthethine, cysteamine, or EGCG. The rejection fails to identify any disclosure in Coggeshalle of any such combination. Thus, each and every element of claims 13, 14 and 15 is not disclosed by Coggeshalle. Accordingly, the rejection is deficient as a matter of fact and law and should be withdrawn.

c. Fine

Claims 9 and 10 were rejected under 35 USC § 102(b) as anticipated by Fine, U.S. Patent No. 6,203,819 ("Fine"). (Paper No. 20070723 at 8). In making the rejection, the Examiner asserted that, "Fine discloses a supplement comprising lipoic acid and biotin . . . in a method that assists in the metabolism of glucose for patients with diabetes and pre-diabetes." (*Id.*)

With a view towards furthering prosecution, claims 9 and 10 have been cancelled. Accordingly, the rejection has been rendered moot and should be withdrawn.

Obviousness Rejections

a. Gorsek

Claims 3 and 4 were rejected under 35 USC § 103(a) as obvious over Gorsek, U.S. Patent No. 6,103,756A, issued August 15, 2001 ("Gorsek"). (*Id.* at 9). For the reasons set forth below, the rejection is respectfully traversed.

In making the rejection, the Examiner asserted that "Gorsek discloses a supplement formulation comprising biotin and pantothenic acid for the treatment of **diabetic retinopathy, a complication of diabetes**..." (*Id.*, emphasis added.) The Examiner acknowledged, however, that the Gorsek formulation "lacks pantethine." (*Id.*) To fill the acknowledged gap, the Examiner asserted that because "[p]antethine is a metabolite of pantothenic acid"..., "it would have been obvious ... to replace pantothenic acid with the metabolite pantothene in a combination of biotin with the pantethine because one would expect that they would have equivalent activity." (*Id.* at 9-10).

It is well settled that the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the documents relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731-32 (2007) (the obviousness "***analysis should be made explicit***" and the teaching-suggestion-motivation test is "***a helpful insight***" for determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to combine documents must be thorough and searching. And, as is well settled, the

teaching, motivation, or suggestion to combine "***must be based on objective evidence of record***." *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added).

Gorsek discloses a formulation comprising various ingredients referred to by Gorsek as the "essential ingredients" (Gorsek, col. 1, line 56). These **"essential" or required ingredients** are identified as follows:

> 100-6000 mg Vitamin C;
> 100-2000 IU Vitamin E;
> 100-20,000 IU Vitamin A;
> 100-1000 mg Magnesium;
> 100-3000 mg L-Taurine;
> 50-600 mg Selenium;
> 40-1000 mg Bilberry extract;
> A natural fruit, with standardized 10-50% anthocyanosides;
> 6-100 mg Lutein extract;
> 6-100 mg Lycopene extract;
> 50-1000 mg alpha lipoic acid;
> 10-1000 mg Quercetin;
> 10-1000 mg Rutin; and
> 10-1000 mg citrus bioflavonoids.
>
> (*Id.* at Col. 1, lines 56-65).

Noticeably absent from the list of ingredients that Gorsek identifies as "essential" to his formulation, are both biotin and either pantothenic acid or its metabolite pantethine.

Gorsek further discloses that **"[i]n addition to these components, at least one compound selected from the group consisting of** Vitamin D3, thiamine,

riboflavin, niacin, Vitamin B6, folic acid, Vitamin B12, biotin, pantothenic acid, Calcium, Iodine, Zinc, Copper, Manganese, Chromium, Molybdenum, N-acetyl-cysteine, plant enzymes, biopene, malic acid, L-glycine, L-glutathione and Boron **can be added in effective amounts**." (*Id.* at Col. 2, lines 1-8).

Gorsek thus lists optional components, each of which may or may not be combined with **all of the "essential" ingredients** listed above. *See, e.g.*, Table 1 for an exemplified formulation. Gorsek does not provide any guidance in how to select from these optional ingredients. Further confirming the apparently limitless options for the formulation, Gorsek discloses that one skilled in this art "can easily modify or change the formulation . . . to provide an unique desired product." (Col. 2, Ins. 25-28). Given the essentially limitless options for modifying the Gorsek formulation, we respectfully submit that the rejection identifies no basis for selecting pantothenic acid, let alone pantothine as claimed, from the large number of possibilities. But, as is well settled, that was the Examiner's burden. *See, e.g., In re Petering*, 301 F.2d 676, 683 (CCPA 1962) (a genus does not render a species obvious) and *In re Baird*, 16 F.3d 380, 383 (Fed. Cir. 1994).

It is also noted that Gorsek's formulations are reported to be effective for **eye conditions**: "age related macular degeneration, cataracts, elevated ocular pressure, diabetic retinopathy and glaucoma." (Gorsek, col. 1, lines 6-8). Gorsek does not disclose the use of the formulation for treating the **underlying diabetes itself** as disclosed in the present application and recited in, e.g., claim 26. Thus, one of ordinary skill in the art would not look to Gorsek for information relating to formulations or

methods for treating or preventing diabetes. Nor does the Examiner provide any evidence or even any argument why one would look to a disclosure for the treatment of eye conditions for diabetes.

We further note that Gorsek provides no data to support its contention that its formulation is effective to treat or prevent anything including eye diseases as claimed in Gorsek, let alone diabetes as claimed in *e.g.*, claim 26 of the present invention. Accordingly, the Gorsek formulation is not enabled and, therefore, is not properly citable against the present claim. *In re Kumar*, 418 F.3d 1361, 1368 (Fed. Cir. 2005) ("Although published subject matter is 'prior art' for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention."); *Minnesota Mining and Manufacturing Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301, 64 USPQ2d 1270, 1278 (Fed. Cir. 2002) ("the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation").

Therefore, for all the reasons set forth above, it is respectfully submitted that the Examiner's rejection is insufficient and should be withdrawn.

b. Reddi and Cincotta.

Claims 1-4, 26 and 27 were rejected under 35 USC § 103(a) as obvious over Reddi and Cincotta *et al.*, U.S. Patent No. 5,714,519, Issued February 3, 1998 ("Cincotta"). (Paper No. 20070723 at 10). For reasons set forth below, the rejection is respectfully traversed.

In making the rejection, the Examiner asserted that Reddi discloses "the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice..." (*Id.*) The Examiner acknowledged, however, that Reddi does not disclose "the use of pantethine or cysteamine in the treatment of diabetes." (*Id.*) The Examiner asserted that Cincotta discloses "the administration of panthethine ... or cysteamine ... for the treatment of hyperglycemia, glucose intolerance, insulin resistance and hyperinsulinemia but lacks biotin." (*Id.*) The Examiner then cited *In re Kerkhoven* for the proposition that "[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose." (*Id.*) Thus, the Examiner concluded that it would have been obvious to one of ordinary skill in the art to combine biotin with either panthethine or cysteamine for the treatment of diabetes. (*Id.*)

Initially, we note that with a view towards furthering prosecution, claims 2 and 27 have been cancelled. Therefore, the rejection is moot with respect to those two claims and should be withdrawn.

As is well settled, "references that teach away cannot serve to create a prima facie case of obviousness." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1131, 1132 (Fed. Cir. 1994). If references taken in combination would produce a "seemingly inoperative device," the CCPA has held that such references teach away from the combination and thus cannot serve as predicates for a prima facie case of obviousness. *In re Sponnoble*, 405 F.2d 578, 587, 160 USPQ 237, 244 (CCPA 1969) (references teach away from combination if combination produces seemingly inoperative device);

see also In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984) (inoperable modification teaches away). "...[W]hen the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007).

It is respectfully submitted that one of skill in this art would view Reddi as teaching away from the instantly claimed invention. Reddi used KK mice as a model of diabetes and administered a low dose (2 mg/kg) and a high dose (4 mg/kg) biotin to these mice. Applicants note that the high dose Reddi used is higher than and is outside of the range claimed by Applicants. But even with such a high dose of biotin, Reddi did not find it useful in db/db models of diabetes or in streptozotocin-induced diabetic rats. As disclosed by Reddi, "Our...results indicate that high-dose biotin treatment does not lower blood glucose levels in...genetically obese diabetic (db/db) mice." (Reddi, p. 1329). With this statement from Reddi, one skilled in this art would not expect that biotin works on db/db mice. In contrast, the present specification discloses that the present biotin-containing compositions unexpectedly exert a synergistic effect on the glucose removal rate in db/db mice. Thus, Reddi unambiguously teaches away from the currently claimed invention. For this reason alone, the rejection should be withdrawn.

Further, applicants have shown unexpected synergistic results achieved by combinations of biotin with other compositions. Contrary to Reddi's findings, combinations of biotin and phytanic acid synergistically lower glucose levels, beyond the additive effects of biotin and phytanic acid. Similarly, biotin in combination with

cysteamine and EGCG as claimed show synergistic de-activation of genes associated with glucose metabolism. (Example 13). Nothing in either Reddi or Cincotta hints at or suggests that such a benefit could be obtained by combining biotin and panthethine or cysteamine. Thus, the presently claimed compositions comprising biotin and panthethine or cysteamine and the method of using same provides unexpected and superior results, which would not have been obvious to the skilled artisan. Accordingly, for this additional reason, it is respectfully requested that this rejection be withdrawn.

c. Reddi and Fleuhmann

Claims 1, 2, 7, 8, 26 and 27 were rejected under 35 U.S.C. § 103(a) as obvious over Reddi and Fleuhmann *et al.*, European Patent Application EP 1177789 A2, published February 6, 2002) ("Fleuhmann"). (Paper No. 20070723 at 10-11.) In making this rejection, the Examiner asserted that "Reddi *et al.* describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of phytanic acid in the treatment of diabetes. Fluehmann *et al.* teaches the use of ***phytanic acid derivatives*** for the treatment and prevention of diabetes or other conditions associated with impaired glucose tolerance (paragraphs 24 and 25) but lacks biotin." (*Id.* at 11). The Examiner then concluded that it would have been obvious to one of ordinary skill in the art to combine biotin and phytanic acid for the treatment of diabetes. (*Id.*)

With a view towards furthering prosecution, claims 2, 7, 8 and 27 have been cancelled. Furthermore, claims 1 and 26 have been amended to delete all recitations to "phytanic acid." With this amendment, the combination of Reddi and

Fluehmann is left with a gap, which renders the rejection untenable with respect to amended claims 1 and 26. Therefore, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

d. Reddi and Wessel

Claims 1, 2, 9, 10, 26 and 27 were rejected under 35 U.S.C. 103(a) as obvious over Reddi and Wessel *et al.*, US patent No. 6,117,899, issued September 12, 2000 ("Wessel"). (Paper No. 20070723 at 11-12). In making this rejection, the Examiner asserted that "Reddi *et al.* describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of lipoic acid in the treatment of diabetes. Wesell *et al.* teaches the use of R-(+)-α-lipoic acid (col. 2, lns. 35-37) as an antidiabetic drug but lacks biotin." (*Id.*) The Examiner then concluded that "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention...to combine biotin and lipoic acid for the treatment of diabetes." (*Id.* at 12).

With a view towards furthering prosecution, claims 2, 9, 10 and 27 have been cancelled. Furthermore, claims 1 and 26 have been amended so that they no longer recite "lipoic acid." With this amendment, the combination of Reddi and Wessel is left with a gap, which renders the rejection untenable with respect to amended claims 1 and 26. Therefore it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

e. Reddi and Van Leare

Claims 1, 2, 5, 6, 26 and 27 were rejected under 35 USC 103(a) as obvious over Reddi and Van Leare *et al*, US Patent Application No. 09/990,937 ("Van Leare"). (Paper No. 20070723 at 12-13). For reasons set forth below, this rejection is respectfully traversed.

In making the rejection, the Examiner asserted that Reddi discloses "the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice..." (*Id.* at 12.) The Examiner acknowledged, however, that Reddi does not disclose "the use of epigallocatechin gallate (EGCG) in the treatment of diabetes." (*Id.*) The Examiner asserted that Van Leare discloses "the use of a green tea extract containing 20 wt. % catechins expressed as epigallocatechin gallate in a dietetic preparation for **inhibiting intestinal absorption** of carbohydrates but lacks biotin" and that "[d]ecreased absorption of carbohydrates can be beneficial to diabetics (pg 1, paragraph 3)." (*Id.*, emphasis added) The Examiner then cited *In re Kerkhoven*, for the proposition that "[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose." (*Id.* at 12-13) Thus, the Examiner concluded that it would have been obvious to one of ordinary skill in the art to combine biotin and epigallocatechin gallate for the treatment of diabetes. (*Id.*)

Reddi has been summarized above. For brevity, we highlight below certain deficiencies in Reddi with respect to the present rejection. Reddi teaches away: one of ordinary skill in the art would read Reddi with the contrary results in db/db mice

and streptozotocin-induced diabetic rats, and dismiss this document rather than repeating his experiments in the hope of achieving a different, positive result. For this reason alone, the rejection should be withdrawn.

Furthermore, as mentioned previously, Reddi does not suggest that biotin in combination with any substance would show unexpected synergistic results. Similarly, Van Leare is silent as to the combination of biotin and EGCG.

Indeed, Van Leare discloses 2-hydroxy carboxyllic acids in combination with a carbohydrase inhibitor. (*See, e.g.*, p. 5, para. 59). The Examiner, however, has not - and cannot - identify any disclosure in Van Leare of the use of the carbohydrase inhibitor alone, let alone in combination with biotin. Thus, the record is devoid of any evidence, let alone a reason one skilled would make the combination proposed by the Examiner.

We further note that Van Leare discloses an extremely large genus of carbohydrase inhibitors, particularly exemplifying as "preferred" carbohydrase inhibitors "phaseolamin, roselle tea, lotus, arabinose, inosine, adenosine, evening primrose extract, banana extract, undigestible dextrin and polyphenols." (*See*, p. 5, para. 59). Van Leare exemplifies certain polyphenols including catechins or derivatives thereof, anthocyanidins, proanthocyanidins, procyanidin and cyandin. Given the extreme breadth of the genus (and subgenus) disclosed by Van Leare for its "carbohydrase inhibitors," the rejection should have, but did not, identify any disclosure or reason to select a single species of "carbohydrase inhibitor - ECGC - over all the rest of possible species. But that was the Examiner's burden. *See, e.g., In re Petering*, 301 F.2d 676,

683 (CCPA 1962) (a genus does not render a specimen obvious) and *In re Baird*, 16 F.3d 380, 383 (Fed. Cir. 1994). For this reason also the rejection should be withdrawn.

We also note that the instant application discloses that the combination of biotin and EGCG would exert a synergistically beneficial effect in gene expression levels, as measured by the Affymetrix GeneChip method. (Example 13). The combination showed that there is a synergistic down-regulation of the glucose-6-phosphate complex, which included one of the major glucose-metabolism rate-limiting enzymes. Thus, the presently disclosed and claimed composition (recited in e.g. claim 26) comprising of biotin and EGCG provides unexpected and superior results, which would not have been obvious to the skilled artisan. Accordingly, for this additional reason, it is respectfully requested that this rejection be withdrawn.

Additionally, we respectfully submit that the goal of inhibition of intestinal absorption of carbohydrates as disclosed in Van Leare is not the same as treating or preventing diabetes. Although inhibiting the intestinal absorption of carbohydrates "can be advantageous for subjects suffering [from] diabetes," (Van Leare, col. 1, paragraph 3), "advantageous" does not necessarily mean prevention or "treatment" as recited in, e.g., claim 26. For example, it is well known that diabetic patients suffer from many complications as a result of diabetes, and the alleged "advantage" that Van Leare's disclosure referred to could simply be a treatment for one of the complications, not treatment or prevention of the underlying diabetes itself. Thus, *In re Kerkhoven* does not apply to the instant rejection because the purposes are not the same.

Accordingly, for the reasons set forth above, withdrawal of this rejection is respectfully submitted.

e. Reddi and Crespo

Claims 1, 11, 12, and 26 were rejected under 35 USC 103(a) as being upatentable over Reddi and Crespo *et al.* Int. J. Clin. Pharmacol. Res. 19(4): 117-127 (1999) ("Crespo"). (Paper number 20070723 at 13-14).

In making the rejection, the Examiner asserted that "Reddi *et al.* describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of policosanol in the treatment of diabetes. Crespo *et al.* describes the use of policosanol for the treatment of dyslipidemia associated with Type 2 diabetes (p. 188, col. 2, lns. 30-41) but lacks biotin. "The Examiner also asserted that" "Dyslipidemia is associated with both Type 1 and Type 2 diabetes and results in an increase in the relative risk of coronary heart disease in comparison to the nondiabetic population (Best and O'Neal, *Drugs*, 59(5), p. 1101-1111, 2000)."

The Examiner then concluded that it would have been obvious "to one of ordinary skill in the art to combine biotin and policosanol for the treatment of diabetes." (*Id.* at 14).

With a view towards furthering prosecution, claims 11 and 12 have been cancelled, and claims 1 and 26 have been amended to delete all recitation to policosanol. With the amendment to claims 1 and 26, the combination of Reddi and

Crespo is left with a gap, which renders the rejection untenable as to amended claims 1 and 26. In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

f. Reddi and Pearson

Claims 18 and 19 were rejected under 35 USC § 103(a) as obvious over Reddi and other documents (as applied to claims 1-12 above) and further in view of Pearson *et al.*, U.S. Patent No. 6,261,589 B1 ("Pearson"). (Paper No. 20070723 at 14). For reasons set forth below, this rejection is respectfully traversed.

In making the rejection, the Examiner asserted that "Reddi *et al.* describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of policosanol in the treatment of diabetes. Crespo *et al.* describes the use of policosanol for the treatment of dyslipidemia associated with Type 2 diabetes (p. 188, col. 2, Ins. 30-41) but lacks biotin. "The Examiner also asserted that" "Dyslipidemia is associated with both Type 1 and Type 2 diabetes and results in an increase in the relative risk of coronary heart disease in comparison to the nondiabetic population (Best and O'Neal, *Drugs*, 59(5), p. 1101-1111, 2000)."

Initially, we note that the rejection is deficient as a matter of law. The rejection states that it is based on "Reddi *et al.* as applied to claims 1-12 above." (Paper No. 20070723 at 14). There is no single rejection based on Reddi alone or in combination with other documents that rejects "claims 1-12." Thus, it is unclear what document or documents, other than Reddi and Pearson, that the Examiner is relying on.

This is unfair and improper. The Applicants should not have to guess at or try and reconstruct the Examiner's rejection. MPEP § 706.02(j) ("It is important for an examiner to properly communicate the basis for a rejection so that the issues can be identified early and the applicant can be given fair opportunity to reply."). Indeed, as the MPEP recognizes, it is the Examiner's burden to present a full and clear rejection. (*Id.*) When this is not done, the rejection is improper and cannot stand. For this reason alone, the rejection should be withdrawn.

Notwithstanding the foregoing, and in an attempt to further prosecution, as understood, the rejection relies on Cincotta, Floehmann, Wessel, Van Leare, Crespo, as well as, Reddi and Pearson. If this is incorrect, the Examiner is requested to reissue the Office Action and explicitly identify the documents relied upon to reject Claims 18 and 19.

In making the rejection, as understood, the Examiner asserted that as previously described, "combinations of biotin with panthethine or cysteamin[e], EGCG, phytanic acid, lipoic acid or policosanol are obvious combinations." (*Id.*) The Examiner acknowledged, however, that none of the documents cited disclose "the use of the composition in a beverage." (*Id.*) To fill the acknowledged gap, the Examiner asserted that Pearson discloses a composition "in solution (as a soft drink) to support the production of and to stimulate the release of **neurotransmitters and neuromodulators in the brain**...but lacks biotin in combination with panthethine or cysteamin[e], EGCG, phytanic acid, lipoic acid or policosanol." (*Id.*, emphasis added). The Examiner then concluded that "it would have been obvious to someone of ordinary skill in the art at the

time of the instant invention to use the nutraceutical of the instant case in a beverage to achieve the physiological effect of the supplement." (*Id.*)

We adopt and reassert our arguments here as if recited in full. Briefly, we observe that Reddi (either alone or taken in view of the other documents, *supra*) does not teach nor suggest the compositions (and methods) recited in the claims as amended. As demonstrated above, Reddi in combination with the other documents cited by the Examiner in the previous rejections were factually and legally deficient to support any rejection under § 103 to any of the claims. And, the addition of Pearson has not remedied the legal deficiencies and factual gaps. Thus, the rejection of claims 18 and 19 should be withdrawn for this reason alone.

In addition, as the Supreme Court in *KSR* stated, the obviousness "analysis should be made explicit." *KSR*, 127 S.Ct. at 1731-32. Respectfully, we submit that the rejection is devoid of *any* evidence - or even argument - in support of the proposed combination. The Examiner reached the opinion that the combination is obvious in a conclusory fashion without providing any motivation for the combination. Therefore, for this additional reason, the rejection should be withdrawn.

Furthermore, we respectfully submit that there is no motivation to combine Pearson with Reddi or any other document cited in the Office Action. Pearson is directed to a composition for producing a positive psychoactive effect which contains a combination of:

phenylalanine
vitamin B-6

vitamin C

folic acid

copper

taurine

choline

vitamin B-5 or pro-vitamin B-5

fruit sugar

optionally the addition of non-caloric natural or artificial sweetener like astevia or spartame

caffeine

optionally green tea

in a carbonated mixture. (Pearson, col. 2, lines 19-26, *see also Id.* at col. 6, lines 11-30).

Pearson discloses that this composition acts by stimulating the release of **neurotransmitters and neuromodulators in the brain** to produce a positive psychoactive effect. (*Id.*, col. 6, lines 31-35). Pearson, which is silent as to 1) diabetes, 2) biotin, and 3) biotin in combination with another active ingredient, is not even remotely related to the compositions recited in claims 18 and 19. For this reason also the rejection fails.

Accordingly, it is respectfully requested that this rejection be withdrawn.

g. Reddi and Holbrook

Claims 18 and 19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reddi and Holbrook *et al.*, U.S. Patent No. 6,132,795 ("Holbrook"). (Paper No. 20070723 at 14-15). For reasons set forth below, this rejection is respectfully traversed.

In making the rejection, the Examiner asserted that "[a]s described above, combinations of biotin with panthethine or cysteamin[e], EGCG, phytanic acid, lipoic acid or policosanol are obvious combinations." (*Id.* at 14). The Examiner acknowledged, however, that none of the documents cited disclose "the use of the composition in a food." (*Id.* at 14-15). To fill the acknowledged gap, the Examiner asserted that Holbrook discloses "the use of an isoflavone containing material and isoflavone depleted vegetable protein composition that may be used in food as a functional ingredient...but lacks biotin and panthethine or cysteamin[e], EGCG, phytanic acid, lipoic acid or policosanol." (*Id.*). The Examiner then concluded that "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the biotin comprising compositions of the instant case in a food to achieve the physiological effect of the supplement." (*Id.*)

Initially, we note that the rejection is deficient as a matter of law. The rejection states that it is based on "Reddi *et al.* as applied to claims 1-12 above." (Paper No. 20070723 at 14). There is no single rejection based on Reddi alone or in combination with other documents that rejects "claims 1-12." Thus, it is unclear what document or documents, other than Reddi and Holbrook, that the Examiner is relying on. This is unfair and improper. The Applicants should not have to guess at or try and reconstruct the Examiner's rejection. MPEP § 706.02(j) ("It is important for an examiner to properly communicate the basis for a rejection so that the issues can be identified early and the applicant can be given fair opportunity to reply."). Indeed, as the MPEP recognizes, it is the Examiner's burden to present a full and clear rejection. (*Id.*) When

this is not done, the rejection is improper and cannot stand. For this reason alone, the rejection should be withdrawn.

Notwithstanding the foregoing, and in an attempt to further prosecution, as understood, the rejection relies on Cincotta, Floehmann, Wessel, Van Leare, Crespo, as well as, Reddi and Holbrook. If this is incorrect, the Examiner is requested to reissue the Office Action and explicitly identify the documents relied upon to reject Claims 18 and 19.

We adopt and reassert our arguments here as if recited in full. Briefly, we observe that Reddi (either alone or taken in view of the other documents, *supra*) does not teach nor suggest the compositions (and methods) recited in the claims as amended. As demonstrated above, Reddi in combination with the other documents cited by the Examiner in the previous rejections were factually and legally deficient to support any rejection under § 103 to any of the claims. And, the addition of Holbrook has not remedied the legal deficiencies and factual gaps. Thus, the rejection of claims 18 and 19 should be withdrawn for this reason alone.

In addition, as the Supreme Court in *KSR* stated, the obviousness "analysis should be made explicit." *KSR*, 127 S.Ct. at 1731-32. Respectfully, we submit that the rejection is devoid of *any* evidence - or even argument - in support of the proposed combination. The Examiner reached the opinion that the combination is obvious in a conclusory fashion without providing any motivation for the combination. Therefore, for this additional reason, the rejection should be withdrawn.

Furthermore, we respectfully submit that there is no motivation to combine Holbrook with Reddi or any other document cited in the Office Action. Holbrook discloses the use of an **isoflavone-containing material** and an **isoflavone depleted vegetable protein** in various foodstuffs. The health benefits of isoflavones, according to Holbrook, are related to cancer, menopausal symptoms, and cardio-protective effects. (Holbrook, col. 2, lines 22-51). Holbrook is silent as to 1) diabetes, 2) biotin, and 3) biotin in combination with another active ingredient, and as such is not even remotely related to claims 18 and 19. For this reason, one of ordinary skill in this art would not look to Holbrook to combine with Reddi and the other documents cited by the Examiner. And neither Reddi alone or in combination with the other documents cited by the Examiner in the previous rejections, if combined with Holbrook as proposed by the Examiner, renders claims 18 and 19 obvious. For each of these reasons alone, it is respectfully requested that this rejection be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on February 7, 2008.

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Respectfully submitted,

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